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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,827	10/23/2001	John Jacob Schwartz	ENZ-004	6161

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,827	SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-97* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jennifer Dunston.

Claims 1-97 are pending in the instant application.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-33, drawn to an engineered chimeric protein comprising a ligand binding domain or detection domain, classified in class 530, subclass 350.

II. Claims 34-35, only as drawn to nucleic acid and vector encoding chimeric protein comprising a ligand binding domain or detection domain, classified in class 536, subclass 23.1 and class 435, subclass 320.1.

III. Claims 36-41, drawn to a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, wherein the target gene has an effect detectable outside the cell, classified in class 435, subclass 325.

IV. Claims 42-44, drawn to an engineered bistable genetic switch comprising a promoter operably linked to an output gene, and a first and second stimulus responsive proteins, wherein at least one of the proteins is a chimeric protein comprising an interaction domain that binds to a DNA sequence and a peptide

that is responsive to a stimulus, wherein the proteins have opposing effects, classified in class 435, subclass 325.

V. Claims 45-50, drawn to an engineered biological logic gate circuit comprising a cell comprising an output gene the expression of which defines at least a first state and a second state, a first and second proteins responsive to input stimuli, wherein both proteins are responsive to a first state and a second state, which is determined by the states of a first and second input, classified in class 435, subclass 325.

VI. Claims 51-66, drawn to an engineered cellular system comprising a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, and a downstream cell comprising a receptor that is responsive to expression of the reporter gene to a change in a property of the downstream cell, classified in class 435, subclass 325.

VII. Claims 67-78, drawn to method of engineering a ligand-responsive or stimulus-responsive chimeric protein, classified in class 435, subclass 91.4.

VIII. Claim 79, drawn to method of engineering a stimulus-responsive chimeric protein using a database, classified in class 435, subclass 91.4.

IX. Claim 80, drawn to method of engineering a stimulus-responsive chimeric protein using a library of nucleic acids, classified in class 435, subclass 91.4.

X. Claims 81-83, drawn to method of detecting a molecule in solution using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to

a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 29.

XI. Claim 84, drawn to method of detecting a disease using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 800, subclass 3.

XII. Claim 85, drawn to method of detecting a disease marker using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 29.

XIII. Claims 87, drawn to method of treating a patient using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, which affects the expression of a reporter gene that reduces viability or reproduction of a malignant or premalignant cell, classified in class 424, subclass 93.2.

XIV. Claims 88, drawn to method of treating a patient using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, which affects the expression of a reporter gene that

exposes a protein plaque to a protease that attacks the protein plaque, classified in class 424, subclass 93.2.

XV. Claims 89-90, drawn to method of treating a patient using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, which affects the expression of a reporter gene that releases a chemical or biochemical species that renders an etiologic agent less harmful, classified in class 424, subclass 93.2.

XVI. Claim 91, drawn to method of monitoring a fermentation process using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 29.

XVII. Claim 92, drawn to method of screening drug candidates using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 29.

XVIII. Claim 93, drawn to method of identifying a nucleic acid using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain

comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 6.

XIX. Claims 94-97, drawn to method of positioning a cell using a sensor cell comprising a chimeric protein comprising an interaction domain that binds to a DNA sequence operably linked to a target gene and a detection domain comprising a peptide that is responsive to a stimulus, classified in class 435, subclass 375.

Claim 86 link(s) inventions of Groups XII-XIV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 86. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

The products of Groups I-VI are chemically, biologically, and functionally distinct from each other and thus one does not render the other obvious. The product of each group is not needed to produce the products of the other groups (each of which can be isolated from cells or organisms, made synthetically, and/or are self-replicating without the need for the isolated products of the other groups. The chimeric protein of Group I is composed of amino acids, and the Group encompasses proteins not found within the cells of Groups III-VI. The nucleic acid of Group II is composed of nucleotides, which are structurally different than the proteins of Group I and the cells of Groups III-VI. Moreover, the cells of Groups III-VI are structurally distinct from each other in that they are engineered to function as a sensor cell (Group III), bistable switch (Group IV), logic gate circuit (Group V), and a cellular system of an upstream cell and a downstream cell (Group VI). The structure of each of the cells of Groups III-VI are distinct in that they require different chimeric protein and target gene structures and functions to impart the distinct functions of the cells. Therefore, each of the products of Groups I-VI are structurally distinct from each other. Further, each of the groups has a separate utility not shared by any of the other groups. For example, the chimeric protein of Group I has utility in cell free systems. The nucleic acid has utility in expressing proteins *in vivo* or *in vitro*. Each of the cells has different utilities in functioning as a sensor, switch, circuit or a two-cell system. Therefore, the inventions of the groups are capable of supporting separate patents.

The inventions of Groups VII-XIX are biologically and functionally different and distinct from each other and thus one does not render the other obvious. The methods of Groups VII-XIX comprise steps which are not required for or present in the methods of the other groups: identifying one or amino acid sequences that bind a preselected ligand (Group VII), identifying a

stimulus-responsive protein from a database of information (Group VIII), introducing into each of a plurality of cells a nucleic acid from a library of nucleic acids encoding chimeric proteins (Group IX), exposing a sensor cell to a solution comprising a molecule (Group X), administering a sensor cell to a patient, where a change in the chimeric protein of the sensor cells allows detection of the presence of disease in a patient (Group XI), exposing a sample from a patient with a sensor cell (Group XII), administering a sensor cell to a patient, wherein the effect of expression of the reporter gene in the sensor cell reduces viability or reproduction of a malignant or premalignant cell, (Group XIII), administering a sensor cell to a patient, wherein the effect of expression of the reporter gene in the sensor cell exposes a protein plaque to a protease that attacks the protein plaque (Group XIV), administering a sensor cell to a patient, wherein the effect of expression of the reporter gene in the sensor cell renders an etiologic agent less harmful (Group XV), contacting a solution from a fermentation process with a sensor cell (Group XVI), changing the concentration of a drug candidate in contact with a sensor cell (Group XVII), introducing into each of a plurality of sensor cells a library of nucleic acids encoding molecules (Group XVIII), and exposing a sensor cell to a position-dependent stimulus regulating a chimeric protein (Group XIX). The end results of the methods are different: engineering a ligand-responsive or stimulus-responsive chimeric protein based upon the ability of the protein to interact with a ligand or stimulus (Group VII), engineering a stimulus-responsive chimeric protein based upon information retrieved from a database (Group VIII), engineering a stimulus-responsive chimeric protein based upon nucleic acid expression (Group IX), detecting a molecule in solution (Group X), detecting a disease in a patient (Group XI), detecting a disease marker in a sample from a patient (Group XII), treating a patient to reduce the viability or

reproduction of a malignant or premalignant cell (Group XIII), treating a patient to reduce protein plaques (Group XIV), treating a patient to render an etiologic agent less harmful (Group XV), monitoring a fermentation process (Group XVI), screening drug candidates (Group XVII), identifying a nucleic acid using a sensor cell (Group XVIII), and positioning a cell (Group XIX). Thus, the operation, function and effects of these different methods are different and distinct from each other. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents.

Inventions of Groups VII-IX and Group I are related as processes of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by a materially different process, as evidenced by the distinct inventions of Groups VII-IX.

Inventions of Group III and Groups X, XI, XII, XIII, XIV, XV, XVI, XVII, XVIII and XIX are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process, as evidenced by the distinct inventions of Groups X, XI, XII, XIII, XIV, XV, XVI, XVII, XVIII and XIX.

Except for the specific relationships described above, the inventions of Groups I-VI are unrelated to Groups VII-XIX. Inventions are unrelated if it can be shown that they are not

disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different products of Groups I-VI are not used in or made by the methods of Groups VII-XIX.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, the search required for any one group is not required for any other group. Each product requires a separate search of the patent and non-patent literature due to the different structural features of the chimeric protein, nucleic acid or cell. Searching for any of the products will not necessarily identify any of the other claimed products or the claimed methods. The search for each method requires a separate search of the patent and non-patent literature to search the method step(s) not shared with any other group. Therefore, the searches are not coextensive, and the additional searching that is required to search more than one group would impose a serious search burden.

This application contains claims directed to the following patentably distinct species of the claimed invention: engineered chimeric proteins and cells comprising a chimeric protein comprising the following sub-species types:

1. target biomolecule (for example, one of claims 12-14), and

2. interaction domain (for example, one of claims 17, 29 or 31)

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (one combination of elected sub-species types) for prosecution on the merits to which the claims shall

be restricted if no generic claim is finally held to be allowable. Currently, claims 1 and 4 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

> The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.
>
> In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
Art Unit 1636

jad

CELIAN QIAN
PATENT EXAMINER